Mathias Hukkelhoven, PhD
Sr. Vice President, Global Head
Drug Regulatory Affairs

Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080

Tel 862-778-6035
Fax 973-781-5544
Internet:
mathias.hukkelhoven@pharma.novartis.com

STATEMENT OF
MATHIAS HUKKELHOVEN, PH.D.
SENIOR VICE PRESIDENT, GLOBAL HEAD
DRUG REGULATORY AFFAIRS
NOVARTIS PHARMACEUTICALS CORPORATION

BEFORE THE FDA PUBLIC WORKSHOP
SCIENTIFIC CONSIDERATIONS RELATED TO DEVELOPING
FOLLOW-ON PROTEIN PRODUCTS

Rockville, Maryland, September 14-15, 2004

Good morning/afternoon, I am Dr. Math Hukkelhoven, Senior Vice President, Global Head of Drug Regulatory Affairs for Novartis Pharmaceuticals Corporation. I want to thank the Food and Drug Administration ("FDA") for giving me the opportunity to represent the Novartis Group of companies ("Novartis") at this public hearing. The Novartis Group is a world leader in the research and development of products to protect and improve health and well-being. The Group's success as a global leader of the innovator biopharmaceutical industry is demonstrated by the approval and launch of eleven (11) new molecular entities over the last four years – more than any other company.

As today's testimony reflects, FDA is hearing from industry representatives as well as many others who are presenting in many cases essentially two opposite ends of the spectrum on the issue of follow-on biologics. In such a polarized context, Novartis appreciates this opportunity to share an alternative perspective (which we will detail further in our submission to the docket). Our perhaps unique perspective is premised upon several bedrock principles: confidence in scientific progress, the capabilities and experience with biotechnology of our regulatory authorities, as well as the critical importance of patient safety with, and public confidence in, biotechnology-based medicines. We also believe it is important to encourage a competitive marketplace for biotech medicines, as well as chemical drugs, in order to facilitate patient access and continued investment in our industry.

Based upon this foundation, Novartis believes it is time for a regulatory mechanism that encourages the development and approval of follow-on biologics. We define such products as second and subsequent versions of recombinant DNA-derived protein products that depend on the same mode of action, are used in the same indications as the originator product, and are developed based upon an extensive and sound set of data generated by the sponsor, and the demonstration of comparability with an originator product on all relevant levels, i.e., chemical, preclinical, clinical, and immunological.

In suggesting such a new regulatory paradigm, the Novartis Group merely is recognizing the next logical step in the evolution of the biopharmaceutical industry. Its very success and creativity is what makes this step possible. With key patents expiring, the time is appropriate. In proposing that the development and approval of follow-on biologics should be authorized, the Novartis Group is drawing on decades of experience as well as its current capabilities and portfolio across the full breadth of the biotechnology and pharmaceutical industry. While care must be taken and standards maintained, the dramatic progress in biotechnology now enables development of the first follow-on biologic products.

The success of the biopharmaceutical industry deserves comparable regulatory progress

The biopharmaceutical industry has made phenomenal progress since the first biotechnology-based medicine was licensed in the US in 1982. Technologies to make and characterize protein products have progressed rapidly in the last two decades. In the same manner, regulatory requirements need to evolve in line with this development to reflect state-of-the-art science. Thus, as the first generation of biotechnology medicines mature, it is time for a mechanism that encourages the development and approval of follow-on biologics.

Biotechnology medicines have the confidence of the public:

It is essential that the high standards for safety and efficacy that patients expect and that the biopharmaceutical industry has always provided in collaboration with FDA are maintained through appropriate and consistent regulatory requirements for *all* biologics. These standards have been achieved through the application of science-based regulatory requirements. Just as the science has progressed in leaps and bounds over the last two decades, so regulatory requirements need to evolve in line with this development to reflect state-of-the-art science focused on the most appropriate criteria. As recognized by the FDA leadership, it is not appropriate to use outdated regulatory requirements just because those parameters were considered useful historically.

Dr. McClellan, immediate past FDA Commissioner, emphasized the importance of FDA now advancing to promote health. Under Dr. McClellan's leadership at the FDA, the Critical Path report was published, "Innovation Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products." It highlights the opportunity to turn the **art** of drug development into the **science** of drug development (Dr. McClellan's metaphor). As stated in the report, "In many cases, developers have no choice but to use the tools and concepts of the last century to assess this century's candidates," and "…the path to market for even successful candidates is long, costly, and inefficient, due in large part to the current reliance on cumbersome assessment methods".

These themes, which apply to both innovative products and follow-on biologics, highlight the necessity of revisiting all aspects of the progress made with medicinal biotechnology. The time has come to fashion a regulatory paradigm that will apply rigorous scientific criteria to continue ensuring safety and efficacy, while minimizing unnecessary or unethical duplication of preclinical and clinical trials, which waste resources that are needed for continuous innovation and that contribute to artificially high drug costs. We should not be continuing to accumulate regulatory requirements and doing studies simply out of tradition. Industry can and should join now with the Agency to achieve state-of-the-art regulations that correlate with industry's state-of-the-art science.

Stimulate and reward innovation across the full breadth of the biopharmaceutical industry:

The regulations for follow-on biologics should be designed as a series of science-driven requirements that stimulate the industry to become yet more creative and more efficient, and thereby give the most innovative companies the greatest success. Just as the science is not static, our expectations for regulations should not be carved in stone. Biologics are complex molecules that raise specific questions. Where the science is today is not where we will be tomorrow. We cannot and should not design rigid regulatory paths that circumscribe creativity. Instead, we should create straightforward appropriate hurdles that assure the safety of the patient, give some predictability to development, and ensure the availability of effective medicines through biotechnology. Some biologics will be easier to make into follow-ons than others, which may remain forever irreproducible.

Old models and mantras are inhibiting progress – **the product *is no longer* the process**. Choosing worst case scenarios and invoking the Precautionary Principle to defend the status quo is disingenuous. Regulatory paths need to be as dynamic as the products they oversee. The proven capabilities of our regulators must be stimulated to find new mechanisms, revisit old ones, and discard those that no longer contribute to the safety and efficacy of products. The industry, which relies on the confidence FDA approval gives the consumers of our products, can demonstrate confidence in our regulators and work with them using the joint experience of all the stakeholders to design an appropriate route forward. For this reason, the FDA initiative embarked upon by Dr. McClellan to publish a draft Guidance on follow-on biologics should be completed as soon as possible. The draft Guidance will reflect the best current thinking of the agency, and such Guidance is the best foundation for continuing the public debate.

The development of new regulatory requirements must be transparent and the rules fair

For the select few products regulated under the Federal Food, Drug, and Cosmetic Act, there already is an existing pathway under Section 505(b)(2). Whatever regulations ultimately are adopted to enable and encourage follow-on biologics that are regulated outside of Section 505, they must come about through an open process. Biologics are not drugs, and we should not try to force fit them into the generic drugs paradigm. Instead, we should enable discussion of all the issues, from access to innovation, from patents to data exclusivity, and from sponsor obligations to regulatory commitments and perhaps create a "facilitated BLA" or some such appropriate, entirely new, regulatory entity. All these issues can best be addressed in the most open, public process of all – the legislative process of the U.S. Congress. Novartis envisions a win:win solution whereby a follow-on biologics industry is enabled, innovators receive regulatory relief from arcane requirements, and patients get access to high quality and improved biotechnology products at competitive prices. This is not a zero-sum game.

In Conclusion

We must capture the confidence appropriate to the creative and successful biotechnology industry and invite the cumulative experience and ideas of the best and brightest of our legislators, regulators, researchers, industry and consumers in order to devise appropriate legislation to enable a new regulatory mechanism for follow-on biologics. We should expect **all regulatory processes** to be concurrent with scientific progress and not risk leaving patients waiting for life-saving medicines due to unnecessary regulatory demands. Instead, we should think ahead together as to what is needed for

all biologics. Rigorous scientific criteria meeting the highest standards must be applied for both originator and follow-on products.

The new regulatory paradigm must be flexible, developed in a timely manner, and be compatible with the phenomenal rate of scientific progress of biotechnology. It will enable a robust, responsible follow-on biologics industry to develop, stimulate investment into innovation across the industry due to more predictable IP protections resulting in new therapies to meet patient needs, and enable greater access to a broader array of medicines by patients. This is not a time for paralysis based on hysteria and fear, but an opportunity to use the creativity for which the biopharmaceutical industry is known to provide access to yet more safe and effective medicines for patients as effectively and efficiently as possible.

Follow-on Protein Products that are as safe and efficacious as the originator product can be developed based on a comparability approach entailing all relevant levels – if the strategy is chosen correctly and if the science is done properly. Based upon our extensive experience with both drugs and biologics, the Novartis Group of companies have very clear views on general scientific concepts for development and approval of follow-on biologics, and we expect to present those in a submission to the public docket. In the meantime, we support the issuance of regulatory guidance and establishment of legal pathways that maintain the rigorous standards of ensuring product safety and efficacy while at the same time allowing competition after legitimate intellectual property protections have expired.

The Novartis Group looks forward to working with FDA, legislators, colleagues in industry and academia, and the other stakeholders to constructively shape this next critical path for the biopharmaceutical industry. We will very actively support this process to provide solutions that will maintain an incentive for the innovator, while providing access to more affordable medicines for patients.